UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF TEXAS
AMARILLO DIVISION

ALLIANCE FOR HIPPOCRATIC MEDICINE, *et al.*,	§	
Plaintiffs,	§	
v.	§	Case No. 2:22-cv-00223-Z
U.S. FOOD AND DRUG ADMINISTRATION, *et al.*,	§	
Defendants.	§	

INTERVENOR DANCO LABORATORIES, LLC'S MEMORANDUM OF POINTS AND AUTHORITIES IN OPPOSITION TO PLAINTIFFS' MOTION FOR A PRELIMINARY INJUNCTION

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page(s)

Cases:

Page(s)

Page(s)

Page(s)

Statutes:

Regulations:

Page(s)

Other Authorities:

INTRODUCTION

In 2000, after careful analysis of supporting studies and data, the Food and Drug Administration (FDA) concluded that Mifeprex is safe and effective, and approved the drug for use in conjunction with misoprostol. The intervening two-plus decades of use, as well as multiple reevaluations by FDA, have affirmed that conclusion.

Plaintiffs now seek an extraordinary remedy: They ask this Court, decades after the fact, to intercede in the expert federal agency's drug approval process and force FDA to withdraw its approval—a mandatory injunction, in an emergent posture no less. Forcing FDA to withdraw a longstanding approval would seismically disrupt the agency's governing authority as to whether drugs are safe and effective, and would cause Danco direct and immediate harm by shuttering its business. The Court should deny Plaintiffs' request for a preliminary injunction.

To obtain the extraordinary relief of a preliminary injunction, Plaintiffs must show a likelihood of success on the merits, irreparable harm absent an injunction, and that the balance of the parties' interests, and the public interest, warrant relief. *See Nken v. Holder*, 556 U.S. 418, 426 (2009). Plaintiffs can satisfy *none* of these preliminary injunction factors.

Plaintiffs' claims have both procedural and substantive defects that will preclude success on the merits. Start with constitutional standing: No Plaintiff has presented a cognizable injury to the Court. Then consider statute of limitations: It has long since run on Plaintiffs' claims related to the 2000 approval of Mifeprex. On the merits, Plaintiffs face equally high hurdles. They argue that FDA used the incorrect approval pathway to approve Mifeprex. This claim is time-barred as to the 2000 approval and unexhausted as to the 2016 supplemental approval. And in any event, FDA's interpretation of its own regulation is entitled to deference. FDA also did not fail to

consider scientific evidence: FDA has considered on multiple occasions the supposed deficiencies Plaintiffs assert, each time concluding the agency acted properly.

The other *Nken* factors also strongly favor denying a preliminary injunction. The suggestion that *Plaintiffs* will be irreparably harmed if *women* are allowed to continue accessing Mifeprex is meritless. A third party's use of a federally approved drug does not cause organizations or other providers "irreparable harm." That is all the more so when women have been able to lawfully access the drug for over 22 years. In contrast, the consequences for Intervenor Danco Laboratories, LLC from a preliminary injunction, would be existential. Danco is a small pharmaceutical company that distributes one product: Mifeprex. A preliminary injunction forcing FDA to withdraw approval of mifepristone would effectively force Danco out of business. And the public's interest is in retaining access to a drug product that FDA has evaluated to be safe and effective. The public has no interest in a hastily cobbled together, and overtly political, attempt by private parties to wrest control of the drug approval process from the United States agency responsible for it—an agency that has acted deliberately, thoughtfully, and consistent with its authorizing statute and implementing regulations.

Plaintiffs' request for a preliminary injunction should be denied.

FACTUAL BACKGROUND

A. Danco Laboratories LLC and Its Sole Product, Mifeprex®

Danco holds the approved New Drug Application (NDA) for Mifeprex (mifepristone) Tablets, a drug approved by FDA for use in a regimen with misoprostol, for the medical termination of intrauterine pregnancy through 70 days gestation. U.S. Food & Drug Admin., Mifeprex Prescribing Information (Jan. 2023). Mifeprex is Danco's only product.

B. FDA's Approval of Mifeprex In 2000

FDA received the NDA for Mifeprex in March 1996, kicking off a nearly five-year review process. Plaintiffs' App. 527 (hereinafter, "App."). The NDA contained, among other things, data from two multi-center clinical trials involving over two thousand patients, which built on "extensive experience" with the drug outside the US that had shown effectiveness rates from 92.7% to 99%, and two pivotal studies in France. U.S. Food & Drug Admin., Medical Officer's Review of NDA 20-687, at 6-7 (Nov. 1999), https://www.accessdata.fda.gov/drugsatfda_docs/nda/2000/20687_Mifepristone_medr_P1.pdf. In addition to extensive review within the agency, the Mifeprex NDA was the subject of review by FDA's Reproductive Health Drugs Advisory Committee, an outside committee of experts that voted 6-0 (with two abstentions) to recommend approval of the product. App. 518.

In September 2000, after careful review of the extensive data, and consistent with the recommendation from the agency's outside advisors, FDA approved NDA 020687 for the medical termination of intrauterine pregnancy through 49 days' pregnancy. App. 527. This approval necessarily reflected FDA's determination that Mifeprex was safe and effective for the proposed use. 21 U.S.C. § 355(b)(1)(A)(i); *see also id.* § (c)(1)(A), (d); 21 C.F.R. § 314.105(a), (c). The approval was granted under FDA's regulations at 21 C.F.R. Part 314 Subpart H (Subpart H), which permitted FDA to impose conditions the agency deemed necessary to ensure the product's safe use, including in this instance requirements regarding the capabilities and commitments of each healthcare provider who would be authorized to prescribe the drug and restrictions on how the drug would be distributed. App. 527.

Approval under Subpart H is appropriate for drug products that are intended to "treat[] serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over

existing treatments." 21 C.F.R. § 314.500. Where FDA concludes that a drug has been shown to be effective, but "can be safely used only if distribution or use is restricted," Subpart H allows the agency to "require such postmarketing restrictions as are needed to assure safe use of the drug product," which may include restricting distribution to certain facilities or physicians with special training or experience or conditioning distribution on the performance of specified medical procedures. 21 C.F.R. § 314.520(a).

C. 2002 Citizen Petition and FDA Denial

In August 2002, Plaintiffs American Association of Pro-Life Obstetricians and Gynecologists (AAPLOG) and Christian Medical & Dental Associations, along with the Concerned Women for America, submitted a petition requesting, among other things, that FDA stay and ultimately revoke approval of Mifeprex. App. 280. The petition challenged the approval on a number of grounds, including assertions that the requirements for approval under Subpart H were not met and that the data submitted in the NDA did not adequately demonstrate that the drug is safe and effective for the intended use. App. 298-303.

Having "carefully considered the information submitted in [the] Petition," FDA denied the petition in a 33-page response. App. 562. The agency explained in detail that pregnancy can be a serious medical condition and medical abortion provides a meaningful therapeutic benefit over surgical abortion, which is why approval of Mifeprex under Subpart H was appropriate. App. 564-68. FDA also meticulously reviewed, over many pages, how the data in the NDA demonstrated the safety and effectiveness of Mifeprex for the intended use and the agency refuted the petitioners' assertions to the contrary. App. 568-75.

D. Congressional Investigation and GAO Report

In 2008, at the request of several members of Congress, the U.S. Government Accountability Office (GAO) reviewed FDA's approval of Mifeprex and oversight of the drug since approval. U.S. Gov't Accountability Off., *Approval and Oversight of the Drug Mifeprex* (Aug. 2008), https://www.gao.gov/assets/gao-08-751.pdf. The GAO "(1) examine[d] FDA's approach to approving Mifeprex, including the types of evidence considered and the restrictions placed on its distribution and use; (2) compare[d] the approval process for Mifeprex to the approval processes for other drugs approved under the restricted distribution provision of Subpart H; and (3) compare[d] FDA's oversight of the use of Mifeprex since its approval to the agency's oversight of the other drugs approved under the restricted distribution provision of Subpart H." *Id.* at 3-4.

At the conclusion of its 18-month investigation, GAO concluded that the approval process for Mifeprex was consistent with the processes for the other Subpart H restricted drugs and that FDA's postmarket oversight of Mifeprex was consistent with its oversight of other Subpart H restricted drugs. *Id.* at 5-7.

E. Establishment of a Mifeprex REMS

In September 2007, Congress amended the Food, Drug, and Cosmetic Act to give FDA authority to require an applicant to submit a risk evaluation and mitigation strategy (REMS) if the agency determined that a REMS "is necessary to ensure that the benefits of the drug outweigh the risks of the drug." 21 U.S.C. § 355-1(a)(1). This new authority extended to already-approved drugs. 21 U.S.C. § 355-1(a)(2). The enacting statute provided that for already-approved drugs that had in effect elements to assure safe use required under 21 C.F.R. § 314.520 or that the applicant otherwise agreed would be deemed to have an approved REMS in effect, the sponsor would be required to submit a REMS application. Food and Drug Admin. Amends. Act of 2007,

Pub. L. 110–85, tit. IX, § 909(b)(1), (3). FDA subsequently announced that Mifeprex was among the drug products deemed to have a REMS and that would require submission of a REMS application. Identification of Drug and Biological Products, 73 Fed. Reg. 16313 (Mar. 27, 2008).

Danco submitted the REMS application on September 17, 2008, and FDA approved it, as amended, on June 8, 2011. App. 599. The approved REMS maintained and augmented the Subpart H requirements imposed with the initial approval of Mifeprex. App. 604.

F. 2016 Changes to Mifepristone Conditions of Use

In March 2016, FDA approved changes to the Mifeprex indication, doses, and dosing regimen, and revisions to the REMS. App. 616, 625-51. Among other things, Mifeprex was approved for use up to 70 days of gestation; the mifepristone dose was reduced and the misoprostol dose increased, with a change in route of administration from oral to buccal (between the cheek and the gum); the timing of the misoprostol dose was expanded; misoprostol could be taken at home; flexibility was added to the timing and conditions of the required follow-up visit; and it was recognized that qualified healthcare providers other than physicians could prescribe the drug to patients. *Id.*

FDA approved these changes after careful review of clinical and other data demonstrating that Mifeprex would continue to be safe and effective under the revised conditions. App. 630-42. The supporting data primarily included published literature and additional information requested by FDA. *Id.* The submission included information on the efficacy of the revised doses and dosing regimen in over 35,000 women, and at up to 70 days gestation in over 30,000 women. App. 631. Similarly, FDA reviewed extensive information and data from published literature and reported adverse events, including from real-world use of the drug over the 15 years since its approval, to conclude that Mifeprex would be safe under the revised conditions of use. App. 635-42.

In March 2018, responding to another request from several members of the Congress, the GAO issued a report on FDA's actions in approving the 2016 changes. U.S. Gov't Accountability Off., *Information on Mifeprex Labeling Changes and Ongoing Monitoring Efforts* (Mar. 2018), https://www.gao.gov/assets/gao-18-292.pdf. The GAO reviewed FDA policies and regulations, analyzed adverse event reports, reviewed reports from FDA inspections of Danco, examined studies and data related to the safety and use of Mifeprex, and obtained information from a number of sources, including Plaintiffs AAPLOG and the American College of Pediatricians (ACOP) and the National Right to Life Committee. *Id*. at 1, 4 n.12. The GAO concluded that FDA "followed its standard review process when it approved the [2016 changes]." *Id.* at 1.

G. 2019 Citizen Petition and FDA Response

In 2019, Plaintiffs AAPLOG and ACOP submitted a citizen petition to FDA asking the agency to "restore and strengthen elements of the Mifeprex regimen and prescriber requirements approved in 2000," and "retain the Mifeprex [REMS], and continue limiting the dispensing of Mifeprex to patients in clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber." App. 668-69. On December 16, 2021, in a 40-page response addressing in detail petitioners' concerns, assertions, and the sources cited in support, FDA denied the petition, except to the extent the petition generally requested that the mifepristone REMS program continue—which was not at issue. App. 730.

H. Removal of In-Person Dispensing Requirement

One provision of the REMS was a requirement that Mifeprex be provided to the patient in person at the clinic or other healthcare setting in which treatment was delivered. App. 604, 724. On April 20, 2020, citing the implications of the COVID-19 pandemic on the ability (and advisability) of patients' having in-person medical appointments with healthcare providers for this

purpose, the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) sent a letter urging FDA to suspend enforcement of the in-person dispensing requirements of the Mifeprex REMS. App. 710-11.

FDA responded to the letter on April 12, 2021, informing ACOG and SMFM that, based on a review of multiple published clinical studies and postmarketing adverse event reports, the agency had concluded that there were no safety concerns that would preclude suspending the in-person dispensing requirement during the COVID-19 public health emergency. App. 731. Accordingly, during the COVID-19 public health emergency, the agency would exercise enforcement discretion with regard to "dispensing of Mifeprex . . . through the mail either by or under the supervision of a certified prescriber, or through a mail-order pharmacy when such dispensing is done under the supervision of a certified prescriber." App. 734.

I. Plaintiffs' 2022 Lawsuit

Plaintiffs filed this lawsuit challenging as arbitrary and capricious FDA's actions regarding the 2000 approval, denial of their 2002 citizen petition, 2016 supplemental changes, approval of a generic, denial of their 2019 citizen petition, and 2021 non-enforcement decision.

STANDARD OF REVIEW

A preliminary injunction is "an extraordinary remedy" that can be granted only when the moving party "has clearly carried [its] burden of persuasion." *CAE Integrated, L.L.C. v. Moov Techs., Inc.*, 44 F.4th 257, 261 (5th Cir. 2022). In carrying its burden, the movant must show "(1) a substantial likelihood of success on the merits, (2) irreparable injury if the injunction is not granted, (3) that the injury outweighs any harm to the other party, and (4) that granting the injunction will not disserve the public interest." *Id.* (citation omitted). "These four factors are conjunctive — *i.e.*, the plaintiff must cany the burden as to all four factors before a preliminary injunction may be considered." *FirstBank Sw. v. Heartland Fin. USA, Inc.*, No. 2:21-CV-024-Z, 2021 WL 3743806,

at *2 (N.D. Tex. Aug. 24, 2021). Courts are instructed to only invoke their preliminary injunction power "sparingly and only in extraordinary circumstances." *Id.*

ARGUMENT

I. Plaintiffs are Unlikely to Succeed on the Merits of Their Claims.

A. Plaintiffs Lack Standing to Challenge FDA's Approval of Mifeprex.

To establish Article III standing, a plaintiff must have suffered an "injury in fact," meaning an injury to a "legally protected interest which is (a) concrete and particularized; and (b) 'actual or imminent, not conjectural or hypothetical.'" *Tenth St. Residential Ass'n v. City of Dallas*, 968 F.3d 492, 499 (5th Cir. 2020) (quoting *NAACP v. City of Kyle*, 626 F.3d 233, 237 (5th Cir. 2010)). Neither the Organizational Plaintiffs nor the Provider Plaintiffs can show anything close.

1. *The Organizational Plaintiffs Lack Organizational Standing.*

The Organizational Plaintiffs do not have organizational standing for two reasons. First, the only "injury" alleged by the organizations is that the time they have spent challenging FDA's actions have caused them to divert resources from other unspecified activities. Dkt. 7 at 7. These vague allegations do not suffice. And second, contrary to the organizations' suggestion, the administrative act of filing a citizen petition does not confer Article III standing.

An organization has standing in its own right only if it meets the "standing test that applies to individuals." *Tenth St. Residential Ass'n*, 968 F.3d at 500 (citation omitted). An organization can show an injury in fact "by showing that it ha[s] diverted significant resources to counteract the defendant's conduct." *City of Kyle*, 626 F.3d at 238. That showing is not a light lift, however; the defendant's conduct must "significantly and 'perceptibly impair[]' the organization's ability to provide its 'activities—with the consequent drain on the organization's resources.'" *Id.* (citation omitted). And in the Fifth Circuit, any such injury concerning the diversion of resources must be "concrete and demonstrable." *Id.* (citation omitted). An organization that diverts resources in

reaction to a defendant's conduct "does not automatically suffer a cognizable injury in fact." *El Paso Cnty. v. Trump*, 982 F.3d 332, 343 (5th Cir. 2020). Instead, the organization's reaction "must differ from its routine activities." *Id.* at 344. So, to show diversion-of-resources standing, an organization must "identify[] 'specific projects that [it] had to put on hold or otherwise curtail in order to respond to the [challenged laws].' " *Texas State LULAC v. Elfant*, 52 F.4th 248, 253 (5th Cir. 2022) (second and third alteration in original) (citation omitted).

The Organizational Plaintiffs have failed to do so. They say challenging FDA's actions has required them to divert resources away from "other priorities and functions." *See* Dkt. 7 at 7; Dkt. 1-4, ¶ 20; Dkt. 1-6, ¶ 27; Dkt. 1-7, ¶ 21; Dkt. 1-8, ¶¶ 22–23. But they fail to identify any particular "priorities and functions" from which they have diverted resources. Because the Organizational Plaintiffs have not shown that they have "forego[ne] other projects or causes" to challenge FDA's approval of Mifeprex, *Tenth St. Residential Ass'n*, 968 F.3d at 500, they have not established in injury in fact. They have merely alleged a purported "setback to [their] abstract social interests." *Id.* at 500 (quoting *City of Kyle*, 626 F.3d at 239).

OCA-Greater Houston v. Texas, 867 F.3d 604 (5th Cir. 2017), is not to the contrary. Dkt. 7 at 7–8. The Fifth Circuit in that voting-rights case concluded that the plaintiff organization, a group with the mission of "voter outreach and civic education," had sufficiently alleged injury-in-fact where the group had specifically alleged that it had been forced to "calibrate[] its outreach efforts to spend extra time and money educating its members," in "in-depth conversations," about the challenged "provisions and how to avoid their negative effects." 867 F.3d at 610. The need for affirmative outreach because of the allegedly unlawful law, and the corresponding drain on the organization's time and resources from "mitigating [the law's] real-world impact on OCA's members and the public," sufficed to confer standing. *Id.* at 612.

The organizations here make no such claims, nor could they. They are organizations that oppose abortion. *See, e.g.*, Dkt. 1-4, ¶ 9; Dkt. 1-5, ¶ 8; Dkt. 1-6, ¶ 6. They have not alleged that the approval of Mifeprex required them to engage in any "outreach efforts" to educate their members about the impact of Mieprex's approval on their daily lives. 867 F.3d at 610. They thus have not identified, in any concrete or particularized way, any additional time or effort toward mitigating the purported impact of FDA's approval of Mifeprex. *See City of Kyle*, 626 F.3d at 236 (no organizational standing when organization did not explain how their activities differed from "routine lobbying activities"); *Tenth Street Residential Ass'n*, 968 F.3d at 500 (no injury in fact when organization's work aligned with its mission, and the organization did not provide evidence that it had to "forego other projects or causes"); *see also Int'l Acad. of Oral Med. & Toxicology v. FDA*, 195 F. Supp. 3d 243, 257 (D.D.C. 2006) (a "diversion-of-resources injury does not count for Article III purposes") (quotation omitted); *Ctr. for Responsible Sci. v. Hahn*, 809 F. App'x 10, 12 (D.C. Cir. 2020) (no standing to challenge FDA's denial of petition to amend regulations when only allegations were that it would cost time and money for education about animal testing issues). Plaintiffs have merely "conjectured" that the resources that they devoted to challenging FDA could be used for unidentified activities. *City of Kyle*, 626 F.3d at 239. This is not enough.

The Organizational Plaintiffs also suggest they have standing because they have been challenging FDA's actions for "decades," apparently in the form of citizen petitions. Dkt. 7 at 7–8. It is one thing to complain to a federal agency; it is quite another to sue in federal court. FDA doesn't require a showing of injury; a federal court does. The regulation Plaintiffs cite, 21 C.F.R. § 10.45(d)(1)(ii), "does not and cannot confer Article III standing"; a regulation cannot trump the

Constitution.[1] *Physicians for Integrity in Med. Rsch., Inc. v. Comm'r*, No. CV 11-08334 GAF (FMOx), 2012 WL 12882760, at *2 (C.D. Cal. May 23, 2012); *see also Ctr. for Responsible Sci.*, 809 F. App'x at 13 ("Of course, neither Congress nor the FDA can confer a right to judicial review that is not authorized by Article III of the Constitution."); *Pharm. Mfg. Rsch. Servs., Inc. v. FDA*, No. CV 17-04898, 2019 WL 285970, at *4 (E.D. Pa. Jan. 22, 2019) ("Congress cannot abrogate the requirements of Article III.").

2. *The Organizational Plaintiffs Lack Associational Standing.*

The Organizational Plaintiffs next suggest they have associational standing to assert claims on behalf of their members and their members' patients, who allegedly face medical, emotional, and financial harms. Dkt. 7 at 8. Provider Plaintiffs assert similar harms. *See, e.g.*, Dkt. 1-53, ¶ 19; Dkt. 1-51, ¶ 6; Dkt. 1-50, ¶ 15; Dkt. 1-52, ¶ 18; Dkt. 7 at 8. None of these is sufficient.

The alleged harm of treating patients who experience complications from abortion medication does not confer Article III standing. Plaintiffs have not articulated a "particularized" and "actual or imminent" increased risk of harm from such complications or the voluntary reporting of such complications. *Shrimpers & Fisherman of RGV v. Texas Comm'n on Env't Quality*, 968 F.3d 419, 424 (5th Cir. 2020). At most, they have alleged that as with any medication, some small number of patients who voluntarily chose to take the medication have experienced complications. Provider standing, directly or as a member of an Organizational Plaintiff, cannot be based on a third-party patient's independent choice to take Mifeprex. *See Clapper v. Amnesty Int'l USA*, 568 U.S. 398, 414 (2013) (noting the Court's "reluctance to endorse standing theories that rest on speculation about the decisions of independent actors"); *Physicians for Integrity in*

[1] 21 C.F.R. § 10.45(d)(1)(ii) states the FDA's "position" that "[a]n interested person is affected by, and thus has standing to obtain judicial review of final agency action."

Med. Rsch., Inc. v. Ostroff, 670 F. App'x 450, 451 (9th Cir. 2016) (Patients who choose to stop seeing a doctor "are making an independent choice unrelated to the FDA's actions.").[2]

Two individual providers suggest financial losses because they lose the opportunity to render obstetrical and prenatal care to, and collect fees for that care from, those who make the personal decision to use abortion medication. Dkt. 1-53, ¶ 19; Dkt. 1-52, ¶ 17. This cannot serve as a basis for Article III standing because it (again) relies on the decision of an independent actor—the individual who decides to use Mifeprex. *See Amnesty Int'l*, 568 U.S. at 414.

Nor can the Provider Plaintiffs bring claims on behalf of their patients. "The rule for third-party standing requires the named plaintiff to have suffered an injury in fact and to share a 'close' relationship with third-parties who face an obstacle inhibiting them from bringing the claim on their own behalf." *Planned Parenthood of Greater Tex. Surgical Health Servs. v. Abbott*, 748 F.3d 583, 589 (5th Cir. 2014) (citing *Kowalski v. Tesmer*, 543 U.S. 125, 129–30 (2004)). The Provider Plaintiffs have not suffered an injury in fact, nor have they set forth any allegations suggesting a "close" relationship nor any obstacle their patients face.[3]

Nor, relatedly, do the Organizational Plaintiffs have standing to assert the claims of their *members' patients*. The patients of the members of the organizations are not themselves "members of, or otherwise directly associated with" the organizations. *Pennsylvania Psychiatric Soc. v.*

[2] The tertiary injury Plaintiffs claim from being drawn away from caring for other patients to tend to a hypothetical person experiencing hypothetical adverse effects from a federally approved drug product is not, and has never been recognized as, a basis for constitutional standing (and imagine the floodgates if it were). *Cf Cigar Ass'n of Am. v. FDA*, 323 F.R.D. 54, 64–65 (D.D.C. 2017) (association's members did not have standing based on their alleged harm from having to spend more time "counseling patients and their parents" on the dangers of smoking.).

[3] Provider Plaintiffs cite *June Med. Servs. L.L.C. v. Russo*, 140 S. Ct. 2103 (2020), in claiming standing to assert claims on behalf of their patients. But in cases like *June*, the medical providers were advocating for access to services for patients who decided to use them—not attempting to *limit* access to drugs for patients who decide to use them.

Green Spring Health Servs., Inc., 280 F.3d 278, 287 (3d Cir. 2002). Plaintiffs point to no Fifth Circuit case, and we have found none, that authorizes this kind of tertiary constitutional standing. And in any event, for the Organizational Plaintiffs' members' patients to have standing, they would first need to show that the *members* have standing—which they do not, as already explained.

Plaintiffs' claims about emotional harm fare no better. A plaintiff can only establish injury "based on emotional harm if that alleged harm stems from the infringement of some 'legally protected,' or 'judicially cognizable,' interest that is either 'recognized at common law or specifically recognized as such by the Congress.'" *Al-Aulaqi v. Obama*, 727 F. Supp. 2d 1, 25 (D.D.C. 2010) (citations omitted); *Spokeo, Inc. v. Robins*, 578 U.S. 330, 341 (2016) (considering whether intangible harm has "a close relationship" to harm traditionally "regarded as providing a basis for a lawsuit in English or American courts"). There is no legally protected emotional interest in treating patients who choose to take a legal drug and later say they wish they had not.

Finally, alleged harm from purported increased liability and higher insurance costs for providers does not create Article III standing. Plaintiffs do not claim they faced accusations of malpractice or increased insurance costs in the 20 years the medication has been available, nor have they (or can they) tie any such claims to Mifeprex. *See* Dkt. 1, ¶¶ 310–11; Dkt. 1-6, ¶¶ 23–24. Hypothetical and speculative allegations are not enough. *See Ass'n of Am. Physicians & Surgeons, Inc. v. FDA*, 539 F. Supp. 2d 4, 17, 20 (D.D.C. 2008) ("Although Plan B was available OTC for one full year before plaintiffs filed their amended complaint," plaintiffs did not allege that any doctor suffered a loss of revenue or otherwise support their claim that they had an increased risk of legal liability).

B. The Statute of Limitations Has Expired.

Even if Plaintiffs could clear the Article III bar, they face an additional threshold bar: The statute of limitations for Plaintiffs' claims related to the 2000 Approval has long since expired.

APA challenges "must be brought within six years of the final agency action allegedly causing a plaintiff's injury." *Am. Stewards of Liberty v. Dep't of Interior*, 960 F.3d 223, 229 (5th Cir. 2020), *cert. denied sub nom. Yearwood v. Dep't of the Interior*, 141 S. Ct. 1062 (2021). The statute of limitations here ran in 2006, nearly 17 years ago.

Plaintiffs seek to salvage their claims by arguing the 2016 Supplemental Approval and the 2021 Petition Response "reopened" FDA's 2000 Approval. Dkt. 7 at 11–12. "The 'reopener doctrine' provides that a period for seeking judicial review can begin anew 'when the agency in question by some new promulgation creates the opportunity for renewed comment and objection.' " *Nat'l Mining Ass'n v. Off. of Hearings & Appeals*, 777 F. Supp. 2d 164, 173 (D.D.C. 2011) (citation omitted); *Sierra Club v. EPA*, 551 F.3d 1019, 1024 (D.C. Cir. 2008) ("[T]he time for seeking review starts anew where the agency reopens an issue 'by holding out the unchanged section as a proposed regulation, offering an explanation for its language, soliciting comments on its substance, and responding to the comments in promulgating the regulation in its final form' ").

"The doctrine is 'designed to ensure that when the agency by some new promulgation creates the opportunity for renewed comment and objection, affected parties may seek judicial review, even when the agency decides not to amend the long-standing rule at issue.'" *Am. Forest Res. Council v. Ashe*, 946 F. Supp. 2d 1, 22 (D.D.C. 2013) (citation omitted), *aff'd,* 601 F. App'x 1 (D.C. Cir. 2015). "It applies where the 'entire context' shows that the agency 'has undertaken a serious, substantive reconsideration of the existing rule.'" *Id.* (citation omitted.

Plaintiffs have not cited a single case where a court has applied the reopener doctrine in the context of FDA approving a manufacturer's supplemental new drug application ("sNDA"). "The FDA's approval of a SNDA is a relatively closed process." *Ass'n of Am. Physicians & Surgeons*, 539 F. Supp. 2d at 21. The process does not involve or require any rulemaking, and no

notice-and comment procedures are involved. *See* 21 U.S.C. § 355(b); 21 C.F.R. § 314.70. Plaintiffs cannot point to any "serious, substantive reconsideration" of an existing rule because there was no change to an existing rule—much less a new rule promulgated. *Forest Res. Council*, 946 F. Supp. 2d at 22.

Even if the reopener doctrine could be applied (for the first time, apparently) outside the rulemaking context, Plaintiffs' argument would still fail. FDA cannot simply reopen a previous approval and simply change its mind; it must invoke specific procedures to revoke a previously granted approval. *See* 21 USC § 355(e); 21 CFR § 314.150. The 2016 Supplemental Approval, *see* Dkt. 1-33, for example, was in response to a sNDA that Danco submitted to FDA; it did not substantively alter FDA's 2000 Approval of the NDA. The FDA's 2021 Response rejecting the changes suggested in a citizen petition similarly did not trigger reopening because FDA did not engage in reconsideration sufficient to establish reopening: "when the agency merely responds to an unsolicited comment by reaffirming its prior position, that response does not create a new opportunity for review." *See Sierra Club*, 551 F.3d at 1024.

C. Plaintiffs' APA Claims Are Unlikely to Succeed On The Merits.

Even if Plaintiffs could overcome their standing and statute of limitations challenges, their claims still fail on the merits. Plaintiffs argue that (1) FDA used the wrong approval pathway for its 2000 Approval and 2016 Petition Denial, (2) FDA did not reasonably find Mifeprex safe and effective under the conditions of use prescribed, recommended, or suggested in the proposed labeling, (3) FDA violated federal postal laws, and (4) because FDA should not have approved

Mifeprex in 2000, FDA also should not have approved a generic mifepristone in 2019. Dkt. 7 at 14. Each of these is wrong.[4]

1. FDA Properly Approved Mifeprex Under Subpart H.

Plaintiffs first challenge FDA's application of 21 C.F.R. Part 314 (Subpart H) to approve Mifeprex. Subpart H "applies to certain new drug products that have been studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments." 21 C.F.R. § 314.500. Plaintiffs describe pregnancy as a "physiological state" or "condition," terms they suggest cannot be reconciled with "serious or life-threatening illness[]" or disease. Dkt. 7, at 14–15. In Plaintiffs' view, FDA failed to follow its own regulation in approving Mifeprex and denying the 2016 Citizen Petition.

Plaintiffs are unlikely to succeed on this claim. To begin with, Plaintiffs have no timely, exhausted claim that FDA impermissibly used Subpart H to approve Mifeprex. Plaintiffs raised the issue in the 2002 Citizen Petition, and FDA concluded that Mifeprex was properly approved under Subpart H, Dkt. 1-28 at 3-7. The statute of limitations has since run for Plaintiffs to challenge that approval. Plaintiffs did not raise the issue in their 2019 Citizen Petition. They thus have not exhausted any similar claims related to the 2016 Supplemental Approval. *See* 21 C.F.R. § 10.45.

Even if Plaintiffs had timely raised and exhausted this claim, it is meritless. Before approving Mifeprex under Subpart H, FDA considered "the potential in any pregnancy for serious or life-threatening complications—such as hemorrhage—in its determination." App. 565-66; 2008 GAO Report, at 22. FDA's conclusion that Mifeprex met the particular demands of Subpart H was the agency's "official position." *Kisor v. Wilkie*, 139 S. Ct. 2400, 2415–18 (2019) (citing

[4] Because Danco has not sought to intervene on Claim 4, which is related to the 2019 Approval of a generic version of Mifeprex, it does not address the merits of those claims.

Auer v. Robbins, 519 U.S. 452 (1997)). The interpretive inquiry "implicate[s]" FDA's "substantive expertise," *id.*; the agency is the primary arbiter of which drugs are safe and effective for which uses. FDA approved Mifeprex following four years of deliberation and described its rationale in a detailed drug approval package, reflecting that the decision also represents the "fair and considered judgment" of the agency. *Id.*; *see* App. 517-25. The FDA's interpretation is worthy of deference under the modified standard announced in *Kisor*.

Plaintiffs next contend FDA violated its own rule because it considered the avoidance of surgical abortion a "meaningful therapeutic benefit" of Mifeprex. Dkt. 7 at 16–17. Plaintiffs maintain that medical abortions cause more potential serious and life-threatening adverse effects than do surgical abortions, and the necessity of surgical intervention after "many" medical abortions means that Mifeprex is "not an alternative 'therapy' " under Subpart H. *Id.* at 16.

This legal conclusion rests on two incorrect factual premises, both easily disproven (and both within FDA's expertise, not a court's). First, medical abortion is not far more dangerous than surgical abortion. *See, e.g.*, Nat'l Acads. of Scis., Eng'g & Med., *The Safety and Quality of Abortion Care in the United States* 55, 60 (2018); Dkt. 1-33 at 10–1. And second, the assertion that "many" women require surgical intervention following a medical abortion is simply false. *See* Kelly Cleland *et al.*, *Significant Adverse Events and Outcomes After Medical Abortion*, 121 Obstetrics & Gynecology 166, 169 (Jan. 2013), (only 0.06% of patients experienced complications after a medical abortion resulting in hospital admission). FDA's carefully considered decision, rooted in scientific evidence, that Mifeprex confers a "meaningful therapeutic benefit to patients over existing treatments" (here, surgical abortion), 21 C.F.R. § 314.500, was amply supported. App. 566-69. Among other things, FDA considered that use of the medical abortion allows women

to avoid undergoing an invasive surgical procedure – including possible complications of anesthesia or sedation and a longer recovery time following the procedure. *Id.*

2. FDA's 2000 Approval, 2016 Changes, and 2021 Petition Response Relied on Valid Clinical Evidence.

Plaintiffs next assert that FDA's original approval of Mifeprex in 2000 and the supplemental approval in 2016 were arbitrary and capricious because the clinical trials on which FDA relied did not study the exact conditions of use under the approved label. Dkt. 7 at 18. Plaintiffs also claim the 2021 Non-Enforcement Decision and 2021 Petition Response were arbitrary and capricious because the data sources on which FDA relied are invalid.[5]

To begin with, and again, FDA is the expert agency charged by Congress with reviewing and approving drug applications and any subsequent changes to those applications. A team of experts (including physicians, statisticians, chemists, pharmacologists, and other scientists) reviews each NDA submitted to the agency and carefully assesses all relevant data in light of the proposed labeling and intended use of the drug, and supports approval of the application if the applicant has demonstrated that the drug is safe and effective under the conditions of use prescribed, recommended, or suggested in the proposed labeling. Plaintiffs' attack on FDA's rigorous approval process is the quintessential example of a meritless APA challenge. *See Zeneca, Inc. v. Shalala*, 213 F.3d 161, 170 (4th Cir. 2000) (FDA did not act "arbitrarily and capriciously" when it approved an ANDA); *Upjohn Mfg. Co. v. Schweiker*, 681 F.2d 480, 484 (6th Cir. 1982) (rejecting challenge to NDA approval)

[5] Plaintiffs argue in their Memorandum in Support of Preliminary Injunction that the FDA's 2021 Non-Enforcement Decision is arbitrary and capricious because it relied on faulty data. Dkt. 7 at 19. This claim is not included in any Count of their Complaint. *See* Dkt. 1 at 94-110. Plaintiffs only assert one claim based on the 2021 Non-Enforcement Decision—Count 5, which relates only to mailing of mifepristone. For that reason, too, Plaintiffs' argument should be rejected.

And in any event, Plaintiffs' out-of-bounds attack reads a requirement into the law that does not exist. FDA is not limited to relying on data evaluating the exact, proposed conditions of use. Rather, FDA must find that there is "substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling." 21 U.S.C. § 355(d); *see also* App. 589 (explaining to AAPLOG and CMDA that "[m]any clinical trial designs are more restrictive . . . than will be necessary or recommended in postapproval clinical use; this additional level of caution is exercised until the safety and efficacy of the product is demonstrated").

Here, FDA derived the necessary effectiveness and safety data for the 2000 Approval from a U.S. clinical trial and two French trials. App. 519. FDA also repeatedly considered each of the suggested additional restrictions of use Plaintiffs raise here—and repeatedly concluded Mifeprex is safe and effective for patient use without them. *See, e.g.*, App. 522 (FDA "carefully considered" the role of ultrasound and concluded it should be left to the "medical judgement of the physician"); App. 579-80 (same); App. 522 (provider either must be in position to furnish surgical intervention or provide a referral, and proposing monitoring study to ensure quality of care); App. 580-82 (same); App. 522 (travel distance requirement was not necessary in light of requirement of "adequate access to emergency services"); App. 520 (recognizing that mandatory observation period was no longer needed because drug causing the basis for it was no longer used).

The same holds true for the 2016 Supplemental Approval. FDA again concluded that Plaintiffs' proposed limitations were not necessary for Mifeprex to be used safely and effectively. *See* App. 740-41 (reaffirming conclusion to leave to provider judgement whether an ultrasound was required); App. 741 (again recognizing that providers must be able to provide surgical care or have a referring relationship); *id.* (noting that it is "common practice for healthcare providers to

provide emergency care coverage for other healthcare providers' patients"). Plaintiffs' challenges to the 2021 Changes fare no better. They suggest FDA improperly relied on the FDA Adverse Event Reporting System (FAERS) data in reaching its conclusions, and note that FDA acknowledged some limitations in the literature. Dkt. 7, at 20. But the agency need not show *uniform* evidence to support its scientific conclusion; that would be a near-impossibility. It need only determine that substantial evidence supports the agency determinations and decision, which it clearly did; FDA relied on significant published literature in reaching its conclusions. App. 756-765. And while FDA recognized the limitations within the data, it used its expert judgment to reach the conclusion that Mifeprex would be safe and effective under the conditions of use proposed. App. 764.

FDA's repeated, thorough, and well-supported conclusions confirm that the agency's actions were consistent with the statutory and regulatory provisions governing the review and approval of NDAs and were not arbitrary and capricious. *See Cumberland Pharms. Inc. v. FDA.*, 981 F. Supp. 2d 38, 48 (D.D.C. 2013) ("[T]he FDA's judgments as to what is required to ascertain the safety and efficacy of drugs fall squarely within the ambit of the FDA's expertise and merit deference"); *Astellas Pharma US, Inc. v. FDA*, 642 F. Supp. 2d 10, 20 (D.D.C. 2009) (recognizing the "high level of deference that must be afforded to the FDA" in determining methodologies for approval and finding FDA did not act in arbitrary and capricious manner in setting bioequivalence guidelines); *Sanofi-Aventis U.S. LLC v. FDA*, 733 F. Supp. 2d 162, 171 (D.D.C. 2010) (FDA determination of what is necessary to assess purity of generic drug is entitled to deference). Cases where FDA reached the opposite conclusion—that a party had not presented significant evidence that the drug would be safe and effective under the proposed label—are inapposite. *See e.g., United States v. An Article of Device . . . Diapulse*, 768 F.2d 826, 832 (7th Cir. 1985) (affirming

FDA's refusal to permit relabeling of previously condemned medical device). In 2000, 2016, and 2021, FDA considered various issues Plaintiffs raised and, each time, concluded that the approval of the NDA or sNDA was appropriate and that the restricted distribution system and other conditions of use were sufficient to ensure safe use of the product. FDA's decisions, grounded in law and science, must stand.

3. The Approvals Decisions Are Not Contrary to Federal Law.

Plaintiffs also suggest the agency's approvals of Mifeprex are invalid because they did not restrict the distribution of Mifeprex, including through mail. Here, again, Plaintiffs have no exhausted claim. Plaintiffs did not raise arguments about restrictions on the distribution of Mifeprex through mail in any petition at issue in this litigation. The claim should be dismissed on that basis alone. 21 C.F.R. § 10.45.

Plaintiffs are also wrong again on the merits. The Comstock Act does not prohibit the mailing of federally approved drugs when used for a lawful purpose. *See* 46 Op. O.L.C. __, 5 (Dec. 23, 2022), https://www.justice.gov/olc/opinion/file/1560596/download. Plaintiffs' suggestion that the 2000 Approval and 2016 Supplemental Approval are invalid because they "did not include prohibitions on the upstream distribution of mifepristone," Dkt 7 at 21, is also wrong, because it again reads a requirement into the law where none exists. FDA can only impose distribution limitations when it "concludes that a drug product shown to be effective can be safely used only if distribution or use is restricted." 21 C.F.R. § 314.520(a). In 2000, FDA determined that certain restrictions on distribution were necessary to ensure safe use of Mifeprex based on the available data. 2016 Pet. Resp. 19-21. When evaluating the sNDA, FDA considered the subsequent 15 years of data to determine that certain requirements were no longer necessary to ensure safe use of the product. App. 630-42.

II. Plaintiffs Will Not Suffer Irreparable Harm Absent an Injunction.

Plaintiffs bear the burden of showing that the irreparable harm of which they complain is not just possible, but *likely*. *See Winter v. Nat. Res. Def. Council, Inc.*, 555 U.S. 7, 20 (2008). Plaintiffs must face "a significant threat of injury from the impending action," *Dickey's Barbecue Rest. Inc. v. GEM Inv. Grp., L.L.C.*, No. 3:11-CV-2804-L, 2012 WL 1344352, at *4 (N.D. Tex. Apr. 18, 2012) (citation omitted), meaning the injury must be "imminent." *ADT, LLC v. Cap. Connect, Inc.*, 145 F. Supp. 3d 671, 694 (N.D. Tex. 2015). "The 'irreparable harm' factor is perhaps the most important of the four elements that the Court must consider." *Mayo Found. for Med. Educ. & Rsch. v. BP Am. Prod. Co.*, 447 F. Supp. 3d 522, 534 (N.D. Tex. 2020).

For starters, Plaintiffs' extreme delay gives the lie to their arguments about irreparable harm. "[D]elay in seeking a remedy is an important factor bearing on the need for a preliminary injunction." *Wireless Agents, L.L.C. v. T-Mobile, USA, Inc*., No. CIV.A. 3:05-CV-0094D, 2006 WL 1540587, at *4 (N.D. Tex. June 6, 2006) (citation omitted). "Absent a good explanation, a substantial period of delay militates against the issuance of a preliminary injunction by demonstrating that there is no apparent urgency to the request for injunctive relief." *Gonannies, Inc. v. Goupair.Com, Inc.*, 464 F.Supp.2d 603, 609 (N.D. Tex. 2006) (quoting *Wireless Agents,* , 2006 WL 1540587, at *3).

Usually, when a defense of "delay" is made to a preliminary injunction, the parties are quarreling over whether a few weeks' or few months' delay puts a PI out of reach for the complaining party. Here, Plaintiffs seek to undo FDA conduct dating back over *two decades*. The most recent FDA action Plaintiffs point to is the December 16, 2021 citizen petition denial. Dkt. 7 at 6. Plaintiffs then waited *11 months* to file this suit. *See, e.g.*, *Gonannies*, 464 F. Supp. 2d at 609 (six-month delay rebuts any presumption of irreparable harm); *Wireless Agents*, 2006 WL 1540587, at *5 (one-year delay showed "no apparent urgency" to request for injunctive relief).

Even setting Plaintiffs' delay aside, Plaintiffs fail to assert a "significant threat" of imminent injury. Plaintiffs first suggest that "women and girls" may suffer irreparable harm caused by medical abortion. Dkt. 7 at 23. Injuries to third parties are not a sufficient basis for irreparable harm – much less speculative injuries to unknown third parties. *See Alcresta Therapeutics, Inc. v. Azar*, 318 F. Supp. 3d 321, 326 (D.D.C. 2018); *Cardinal Health, Inc. v. Holder*, 846 F. Supp. 2d 203, 213 (D.D.C. 2012). Plaintiffs also point to two extra-record studies sponsored by a prominent anti-abortion organization to support their claimed harm. But here, too, claimed risk of harm is not theirs to claim. These studies are not in the administrative record, and *the agency*, not a court, is the place to submit further studies. 21 CFR § 314.80; 21 U.S.C. 355(k).

Plaintiffs also suggest they will suffer "mental" anguish without a preliminary injunction. But all Plaintiffs assert is a generalized "concern" that members of a provider association will experience "emotional and moral distress." App. 183. This generalized "concern" is too speculative to constitute "irreparable harm." *Digital Generation, Inc. v. Boring*, 869 F. Supp. 2d 761, 784 (N.D. Tex. 2012). If "mental anguish" over a government action sufficed for standing, anyone claiming heartfelt disagreement with, and emotional turmoil caused by, a governmental policy could seek relief. *No* court has ever found irreparable injury in that sort of circumstance.

And finally, Plaintiffs' claims of lost time, money, and resources are not enough to constitute irreparable harm. Dkt. 7 at 23. "Mere injuries, however substantial, in terms of money, time and energy necessarily expended in the absence of a stay, are not enough." *Virginia Petroleum Jobbers Ass'n v. Fed. Power Comm'n*, 259 F.2d 921, 925 (D.C. Cir. 1958).

III. The Harm to Danco and the Public Interest Favors Denying Plaintiffs' Request.

The final remaining factors—balance of hardships and public interest—merge when the government is the opposing party. *Nken*, 556 U.S. at 435. At this juncture, the Court "must balance

the competing claims of injury and must consider the effect on each party of the granting or withholding of the requested relief." *Winter*, 555 U.S. at 24.

Plaintiffs will not be harmed absent an injunction. But even if they were, any alleged harm would be minimal compared to the harm Danco would experience upon entry of a preliminary injunction. Danco is a small pharmaceutical company. It sells one drug: Mifeprex. Danco's App. ¶ 2. Entering the mandatory preliminary injunction Plaintiffs seek would force FDA to withdraw approval for Danco's only product, effectively shuttering Danco's business. *Id.* ¶¶ 2, 4-6. A preliminary injunction should be denied where it "would cause extreme hardship to the business, or even threaten destruction of the business." *Virtus Pharms., LLC v. Garland*, No. CV 21-2308 (CKK), 2021 WL 4306165, at *13 (D.D.C. Sept. 22, 2021) (citation omitted).

Moreover, the type of injunction Plaintiffs seek here is even more unusual than the standard preliminary injunction. "The purpose of a preliminary injunction is merely to preserve the relative positions of the parties until a trial on the merits can be held." *Talon Transaction Techs., Inc. v. StoneEagle Servs., Inc.*, No. 3:13-CV-00902-P, 2013 WL 12173219, at *2 (N.D. Tex. July 24, 2013) (citation omitted). Here, forcing FDA to *withdraw its approval* of mifepristone would not change the status quo; it would completely *upend* the status quo.

The public interest likewise favors denial of a preliminary injunction. The public interest is always supported by allowing patients access to drugs FDA has found to safe and effective. *See Bianco v. Globus Med., Inc.*, No. 2:12-CV-147-JRG, 2012 WL 5611054, at *4 (E.D. Tex. Nov. 15, 2012); *Sandoz, Inc. v. FDA.*, 439 F. Supp. 2d 26, 33 (D.D.C. 2006).

CONCLUSION

For the foregoing reasons, Plaintiffs' motion for a preliminary injunction should be denied.

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Respectfully submitted,

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